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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,998	ECKER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 May 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/28/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on May 07, 2007 has been considered and acknowledged.

Status of the Application

2. Claims 46-90 are currently pending. Claims 1-45 are cancelled. New claims 46-90 are added. All amendments and arguments have been thoroughly reviewed and deemed persuasive in view of amendment. This action is made FINAL necessitated by amendment.

3. The Information Disclosure Statement filed on June 28, 2007 has been considered.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parson et al. (Int J Legal Med., Vol. 111, pp. 124-132, 1998) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996).

Parson et al. teach a method of claim 46, 58, 65, 77, 84, of mitochondrial DNA (mtDNA) analysis comprising (a) (a) providing a forensic evidence sample (see page 131, col. 1, paragraph 1 under case example, page 125, col. 1, line 1-8);

(b) amplifying one or more segment from mtDNA obtained from said sample to obtain one or more amplification products (see page 125, col. 1, paragraph 1 under amplification);

(c) determining molecular masses of said one or more amplification products (see page 125, col. 2, paragraph 1-2 under Results section);

(d) calculating molecular masses of said amplification products and comparing said molecular masses of said amplification products with at least one database comprising plurality of known molecular masses (base compositions) derived from plurality of subjects thereby reaching a forensic conclusion (see page125, col. 2, paragraphs 1-2, table1, indicating comparison with a reference sequence database comprising plurality of known base compositions from plurality of subjects, page 131, col. 1, paragraph 1 under case example).

With regard to claims 51-52, 70-71, Parson et al. teach that said subjects are humans (see page 125, col.1, paragraph 1 under Materials and methods section, page 131, col. 1, paragraph 1 under case example).

With regard to claims 54-55, 73-74, Parson et al. teach that said segment comprises hypervariable region (HV1 and HV2) (see page 125, col. 1, paragraph 2 under Materials and methods).

With regard to claim 56-57, 75-76, Parson et al. teach that generating amplification product from two hypervariable regions using primers flanking said regions and said segments comprise entire mtDNA of the subject (see page 125, col. 1, paragraph under Amplification subtitle).

With regard to claims 59-60, 78-79, parson et al. teach that the forensic conclusion is identification of a criminal or crime victim (see page 131, col. 1, paragraph 1 under case example).

With regard to claim 62, 81, Parson et al. teach that the forensic conclusion comprises analysis of plurality of forensic evidence samples obtained from a plurality of locations (blood, hair from plurality of individuals different locations) (see page 125, col. 1, line 1-6 paragraph 1 under Material and methods, page 131, col. 1, paragraph 1 under case example).

With regard to claim 64, 83, Parson et al. teach that at least one database comprises a Federal Bureau of Investigation mitochondrial DNA database (see page 125, col. 2, paragraph under Armed forces DNA identification laboratory, page 131, col. 1, paragraph 1 under case example).

With regard to claim 84, Parson et al. teach that the method comprises characterizing heteroplasmy of a segment of mtDNA (see page 129, col. 2, paragraph 1, Fig. 3, Fig 4A-4B, page 130, col. 1, line 1-15, paragraph 1-2).

With regard to claim 85, Parson et al. teach that said heteroplasmy is selected from length heteroplsmy, single nucleotide polymorphism (see page 130, col. 1, paragraphs 1-2).

However Parson et al. did not teach determining molecular masses by mass spectrometry.

Aaserud et al. teach a method for accurate measurement of molecular masses of double-stranded DNA by mass spectrometry (see page 1266, abstract, page 1268, col. 1, paragraph 3), wherein Aaserud et al. teach that the method provides accurate molecular weights of its high-resolution mass spectrum from an electrospray ionization/Fourier transform instruments yielding only the correct ds- and ss- base compositions (see page 1266, abstract).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Parson et al. in a manner as taught by Aaserud et al. by incorporating measuring base-composition by mass spectrometry for the purpose of enhancing sensitivity of the method for analyzing sequence variations in said target nucleic acid. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. with a step determining molecular mass measurement by using mass spectrometry as taught by Aaserud et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in a sensitive comparison of base composition variations in mtDNA and accurate measurement of base compositions in said target because Aaserud et al. explicitly taught that the mass spectrometry measures accurate molecular masses thereby providing correct base compositions of a target nucleic acid (see abstract on page 1266) and such modification is considered as obvious over cited prior art.

B. Claims 53 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parson et al. (Int J Legal Med., Vol. 111, pp. 124-132, 1998) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996) as applied to claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 above, and further in view of Oefner et al. (US 6,453,244).

Parson et al. in view of Aaserud et al. teach a method of mtDNA analysis as discussed in the section 4A above.

However neither Parson et al. nor Aaserud et al. teach that the subjects are nonhuman eukaryotic organisms, fungi, parasites or protozoa.

Oefner et al. teach a method for detecting polymorphisms in subjects using PCR- RFLP to identify genetic variability across a population and to provide polymorphism databases for the purposes of forensic identification of an individual or for linkage analysis or population studies (see col. 5, line 6-48, col. 14, line 49-59), wherein Oefner discloses that the subjects include a number of microorganisms including bacteria, parasites and infectious agents like viruses (see col. 14, line 60-67) and analysis of mtDNA (see col. 15, line 6-13).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Parson et al. in a view of Aaserud et al. by incorporating various nonhuman subjects as taught by Oefner for the purpose of analyzing a wide range of populations including nonhuman subjects. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. in view of Aaserud et al. with the method of Oefner because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in analyzing various populations including nonhuman subjects because Oefner explicitly taught that the method provides analysis of genetic diversity and association of the genetic diversity with the disease causing infectious microorganisms, which aid in prognosis of the disease and treatment of individual with the disease (see col. 14, line 60-67, col. 15, line 1-5) and such modification is considered as obvious over cited prior art.

C. Claims 87-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parson et al. (Int J Legal Med., Vol. 111, pp. 124-132, 1998) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996) as applied to claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 above, and further in view of Howell et al. (Am J Hum. Genet., Vol. 66, pp. 1589-1598, 2000).

Parson et al. in view of Aaserud et al. teach a method of mtDNA analysis as discussed in the section 4A above.

However neither Parson et al. nor Aaserud et al. teach that the comparing said heteroplasmy in said sample with at least one database comprising plurality of base compositions from said segment of mtDNA from a plurality of subjects with mtDNA diseases.

Howell et al. teach a method for detecting heteroplasmy in a subject and comparing said heteroplasmy with a mtDNA database comprising plurality of known bases compositions from plurality of subjects with mtDNA disease (Leber hereditary optic neuropathy (LHON)) (see page 1590 col. 2, paragraphs 1-3 under results section, page 1592, col. 1, paragraph 1).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Parson et al. in a view of Aaserud et al. by incorporating association of base composition differences with a mtDNA disease as taught by Howell et al. for the purpose of detecting disesse causing heteroplasmic polymorphisms. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. in view of Aaserud et al. with the method of Howell et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in detecting disease causing polymorphisms or

mutations in mtDNA because Howell et al. explicitly taught that the method provides nalysis of persistent heteroplasmy and mitochondrial hypermutation process which results in mechanistic insights into the expansion/contraction of simple-repeat sequences in relation to mtDNA diseases (see page 1589, abstract) and such modification is considered as obvious over cited prior art.

D. Claims 47-50, 66-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parson et al. (Int J Legal Med., Vol. 111, pp. 124-132, 1998) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996) as applied to claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 above, and further in view of Torroni et al. (Genetics, Vol. 144, page 1835-1850, 1996).

Parson et al. in view of Aaserud et al. teach a method of mtDNA analysis as discussed in the section 4A above.

However neither Parson et al. nor Aaserud et al. teach that digesting amplified PCR products with one or more restriction enzymes to produce restriction fragments before mass spectrometry.

Torroni et al. teach a method of amplifying a segment of mtDNA (see page 1836, col. 1, paragraph 2 under materials and methods section, page 1846, col. 2, paragraph 1); digesting said amplification product with restriction enzymes to produce restriction fragments (see page 1836, col. 1, paragraph 2 under materials and methods section); determining molecular masses of said test restriction fragments (see page 1836, col. 2, line 1-13); and comparing said molecular masses of said restriction fragments with said plurality of known base compositions thereby reaching a forensic conclusion (see page 1839, table 4, page 1840 fig.1, page 1841, fig.2).

Torroni et al. also teach that the restriction enzymes include combination of RsaI, HpaII (see page 1850, legend of Appendix A, page 1836, col. 2, line 1-2).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Parson et al. in a view of Aaserud et al. by incorporating association of base composition differences with a mtDNA disease as taught by Torroni et al. for the purpose of reducing the size of the amplification product. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. in view of Aaserud et al. with the method of Torroni et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in reducing the size of the amplification product because Torroni et al. explicitly taught that the method provides analysis of size variations that reveal polymorphic restriction sites that define mtDNA haplogroups (see page 1836, col. 2, line13, paragraph 2) and such modification is considered as obvious over cited prior art.

E. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over Parson et al. (Int J Legal Med., Vol. 111, pp. 124-132, 1998) in view of Aaserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996) as applied to claims 46, 51-52, 54-65, 70-71, 73-85, 89-90 above, and further in view of Baumer et al. (Am J Hum Genet., Vol. 54, pp. 618-630, 1994).

Parson et al. in view of Aaserud et al. teach a method of mtDNA analysis as discussed in the section 4A above.

However neither Parson et al. nor Aaserud et al. teach analysis of mtDNA from said subject at different ages of the individual to characterize heteroplasmy indicating rate of naturally occurring mutations.

Baumer et al. teach a method for detecting age-related human mtDNA mutations, wherein the method comprises obtaining mtDNA from plurality of tissues at different ages of an individual to detect mtDNA mutations (see page 618, summary, page 621, col. 2, paragraph 2, Fig 2C).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Parson et al. in a view of Aaserud et al. by incorporating association of base composition differences with a mtDNA disease as taught by Baumer et al. for the purpose of detecting naturally occurring mutations.. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Parson et al. in view of Aaserud et al. with the teachings of Baumer et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitation would result in detecting age related mtDNA mutations in an individual with progressing age because Baumer et al. explicitly taught age related accumulation of mtDNA deletions and the progression of mtDNA diseases with the progression of age (see page 618, summary) and such modification is considered as obvious over cited prior art.

Response to arguments:

5. With regard to the objection to informalities to the claim 39, Applicants' arguments and amendment are fully considered and the objection to the claim is withdrawn herein in view of the amendment.

6. With regard to the objection to the Drawings (Fig 20A and 20B) maintained in the previous office action, Applicants' arguments and amendment are fully considered and found persuasive. The objection to the drawings is withdrawn herein in view of the amendment.

7. With regard to the rejection of claims 39-40 under 35 USC 112 second paragraph Applicants' arguments and amendment are fully considered and the rejection to the claims is withdrawn herein in view of the amendment.

8. With regard to the rejection of claims 34-37, 39-40, 43-44 under 35 USC 102(b) as being anticipated by Torroni et al. Applicants' arguments and amendment are fully considered and the rejection to the claims is withdrawn herein in view of the amendment canceling the rejected claims.

9. With regard to the rejection of claims 13, 15-17, 19-20, 22-25, 30-33, 41-42, 45 under 35 USC 103(a) as being obvious over Torroni et al. in view of Aserud et al. Applicants' arguments and amendment are fully considered and the rejection to the claims is withdrawn herein in view of the amendment canceling the rejected claims.

10. With regard to the rejection of claims 18 and 38 under 35 USC 103(a) as being obvious over Torroni et al. in view of Aserud et al. further in view of Oefner, Applicants' arguments and amendment are fully considered and the rejection to the claims is withdrawn herein in view of the amendment canceling the rejected claims.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Prabha Chunduru 8/2/07
SURYAPRABHA CHUNDURU
PRIMARY EXAMINER